Choice of therapy: Patients should be treated with the most potent antiviral agent available. This is to ensure maximal suppression of viral replication. A viral load of less than about 50,000 copies is usually sufficient to prevent progression of disease. However, in order to prevent the development of antiviral resistance the target viral load should be undetectable. Using lamivudine or telbivudine viral loads greater than about 200 copies/ml 6 months after starting treatment indicates inadequate response, and should be a reason to change treatment. With the more potent agents this is less important.
Duration of therapy: Patients who are positive for HBeAg should be treated until 6–12 months after seroconversion. However, since remission may not be durable these patients should be monitored indefinitely after stopping therapy. Patients who are anti-HBe-positive need treatment indefinitely
Combination therapy: As yet there is no data on the use of combination therapy as first line treatment. Possible combinations include one of lamivudine, telbivudine, or entecavir with either adefovir or tenofovir. Lamivudine telbivudine and entecavir should not be used together. Tenofovir and adefovir should not be used together. Truvada is the combination of emtricitabine and tenofovir in a single tablet. Emtricitabine is very similar to lamivudine.
Treatment of antiviral resistance: Patients should be monitored frequently so that if resistance develops it can be caught early. Early treatment of antiviral resistance is more effective than treating resistance one ALT elevation has occurred. Resistance is defined as more than a 1 log increase in viral load assuming good compliance.
Resistance to lamivudine or telbivudine is treated conventionally by adding adefovir. Addition of a second drug is more effective that switching to a second drug. Adefovir, but tenofovir will probably be a better choice in future. It is not known whether tenofovir will require to be used in combination or not. Since patients who develop antiviral resistance to more than one agent have very few if any further options and argument can be made for treating these patients with a combination of tenofovir and entecavir. Resistance to entecavir is treated with adefovir or tenofovir. Resistance to adefovir or tenofovir should be treated with entecavir.
Long term monitoring: Patients with chronic hepatitis B should undergo 6 monthly ultrasound screening for HCC. Patients with known cirrhosis should also have a gastroscopy to look for esophageal varices.

I-77 The host immunity response of hepatitis B patients after adefovir dipivoxil and entecavir therapy

Y.F. Jiang, J.Q. Niu*. *Department of Infectious Disease, First Hospital, Jilin University, Changchun 130021, China*

Background and Aim: Chronic hepatitis B (CHB) is thought to involve aberrant immune tolerance of unknown mechanism. In this study, the immune modulatory effect of adefovir dipivoxil (ADV) and Entecavir (ETV) was determined in CHB patients who are positive for hepatitis B e antigen (HBeAg) based on the efficacy and safety of the Phase IV, randomized controlled trial result.
Methods: 56 CHB patients were treated with ADV or ETV and 24 healthy subjects were used as a control. Two classes of cytokines including IL-2, IFN-γ, TNF-α, IL-4, IL-6, IL-10 and regulatory T cells (Tregs), CD4 and CD8 were measured before treatment and at 12, 24, 36 and 48 weeks after treatment using a three-color flow cytometry. Samples were also tested for HBV DNA, ALT and AST.
Results: In patients treated with ADV or ETV, both Th1 and Th2 cytokines were significantly increased and found to be higher than the controls ($p < 0.01$). The cytokines production was continuously increased along with treatment from weeks 12 up to 48. After 24 weeks of treatment, HBV DNA was greatly reduced among ETV compared to ADV treatment ($p < 0.05$), and high production of IL-2, IFN-γ, TNF-α were observed with ETV compared to ADV treatment. The IFN-γ level at weeks 24 and 48 among patients treated with ETV (16.74±1.34%, 19.78±1.56%) were significantly higher than ADV (7.53±0.55%, 12.56±0.89%) ($P < 0.005$). The IL-2 level at weeks 24 and 48 among patients treated with ETV (10.62±1.11%, 13.14±1.06%) were significantly higher than ADV (5.84±0.46%, 9.46±0.79%) ($P < 0.05$). The TNF-α levels at weeks 24 and 48 among patients treated with ETV (18.35±2.74%, 17.32±1.63%) were significantly higher than ADV (9.96±0.87%, 12.32±1.22%) ($P < 0.05$). Both the proportion of $CD4^+CD25^{high}$ Tregs (3.08%±0.38%) and $CD4^+CD25^+CD127^{low/-}$ Tregs (9.05%±0.69%) were showed a statistically significant increase compared to healthy controls (1.60%±0.66%, $p < 0.01$), (1.92%±0.16%, $p < 0.01$). The Tregs decreased among patients treated with both nucleot(s)ide analogue after week 12 until the 36 week. The CD4/CD8 ratio and the percent of CD4 in CHB were both significantly higher than controls ($p < 0.001$) and the CD4/CD8 ratio were showed a statistically significant decrease compared to the baseline after 24 weeks. IL-6, IL-10, Tregs and the percent of CD4 were associated with HBV DNA levels at week 24, but were independently related to ALT and AST level.
Conclusion: Antiviral therapy with ADV or ETV can increase the Th1/Th2 cytokine secretion in patients with chronic hepatitis B. ETV induced the secretion of IFN-γ more than ADV. The proportion of Tregs decreased after treatment of nucleot(s)ide analogue. Cytokine and Treg play an active role not only in modulating effectors of immune response to HBV infection, but also in influencing the disease prognosis in patients with hepatitis B.

I-78 How to manage and prevent drug resistant HBV

M.F. Yuen*. *The University of Hong Kong, China*

The major limitation of long-term antiviral therapy for chronic hepatitis B is the emergence of drug resistance which negates the benefits of therapy. To minimize the chance of emergence of hepatitis B virus with drug resistance, antiviral agent(s) with rapid and potent viral suppression and high genetic barrier should be the treatment of choice. If an antiviral agent not possessing these properties is used, early measurement of HBV DNA levels should be performed to guide the treatment plan in the subsequent course. Measurement of viral load reduction at 24 weeks of treatment to aid decision making should be mandatory for patients who are receiving antiviral agents with low genetic barrier. Combination therapy for treatment naïve patients using two antiviral agents belonging to different groups is associated with a lower chance of emergence of drug resistance. However, the best choice of combination therapy associated with an acceptable low chance of drug resistance is still being eagerly awaited. With the availability of various antiviral agents from different groups, drug resistant HBV to a particular antiviral agent usually remains susceptible to another antiviral agent of different group. To ensure better control of viral replication in patients with drug resistance, adding on or switching to another antiviral agent with no overlapping resistance profile should be administered as early as possible, e.g. at the time when genotypic resistance emerges.